

Electronic Drug Establishment Registration & Drug Listing in SPL Format

**Drug Information Association SPL Conference
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FDA Data Standards Council



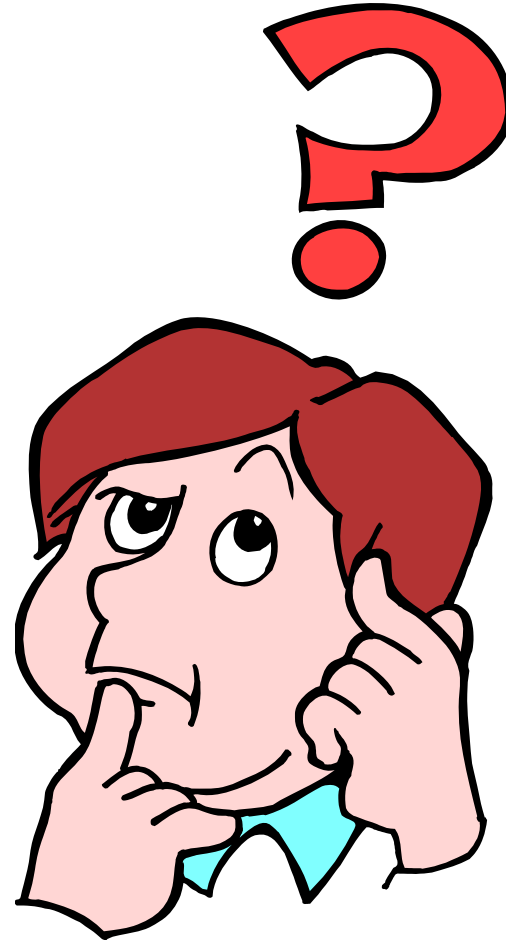
Overview

- Structured Product Labeling (SPL) Standard
- Transitioning from Paper to Electronic Drug Establishment Registration & Drug Listing
- Using SPL Format to Electronically Register Drug Establishments and List Drug Products

The Standard:

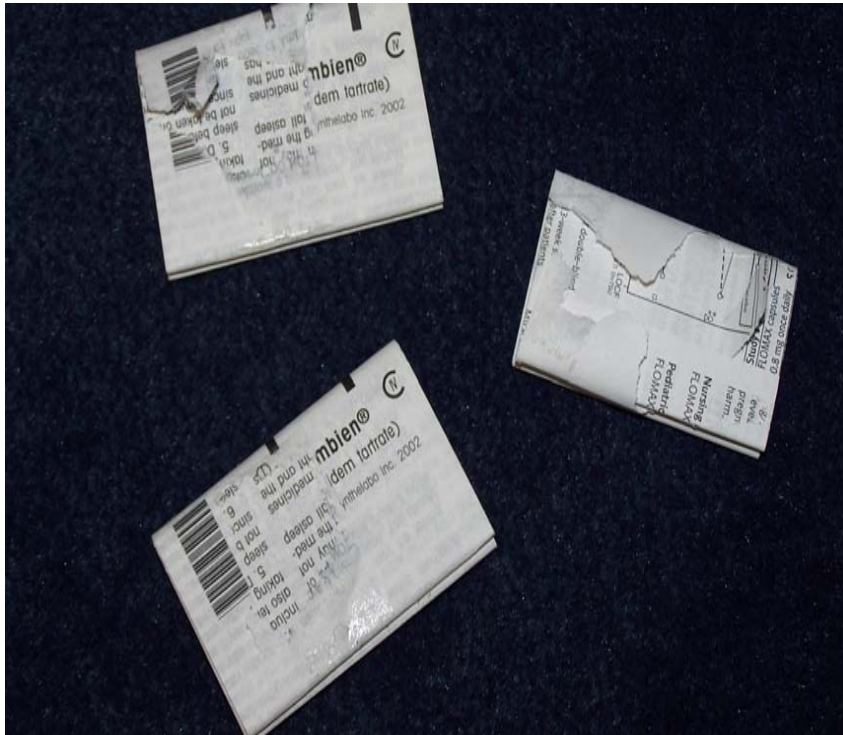
Structured Product Labeling (SPL)

- WHY CHANGE
THE **CONTENT OF**
LABELING THAT
HAS WORKED FOR
DECADES ????

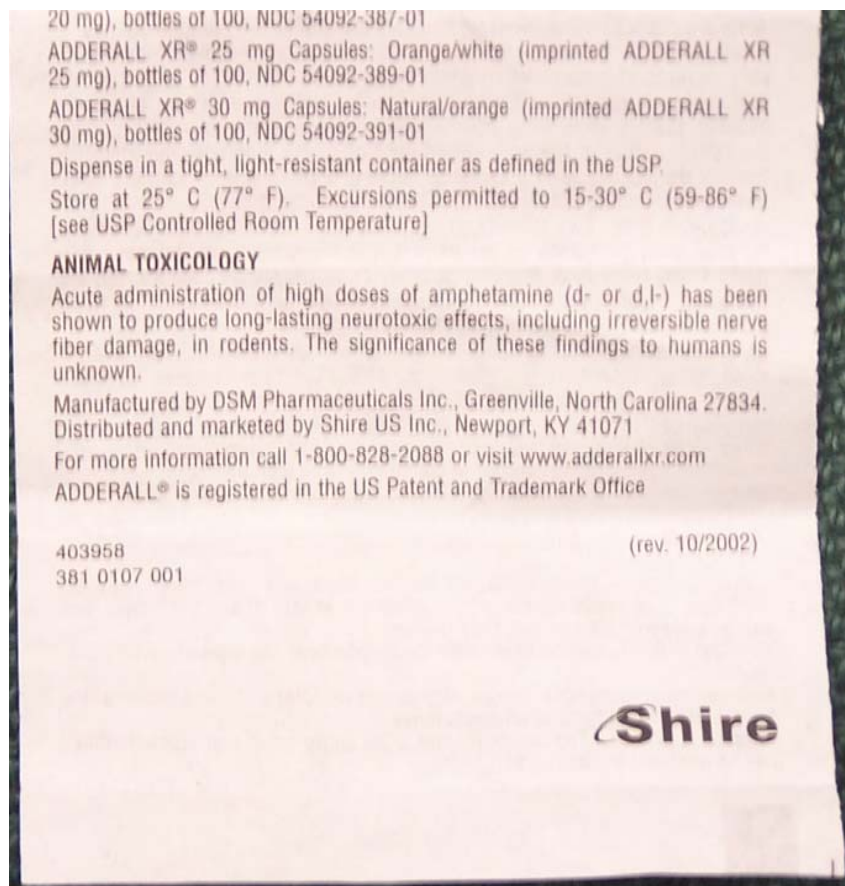




- Difficult to read - Font size and paper shape limits readability and duplication
- Difficult to access – distribution limited (e.g., pharmacy shelf)
- Difficult to use – information in paper labels cannot be accessed by computer systems



- The Labeling Rips when it is Removed!
- Critical data is missing.
- The Product can outdate the Labeling
- The Labeling is Often in the Container



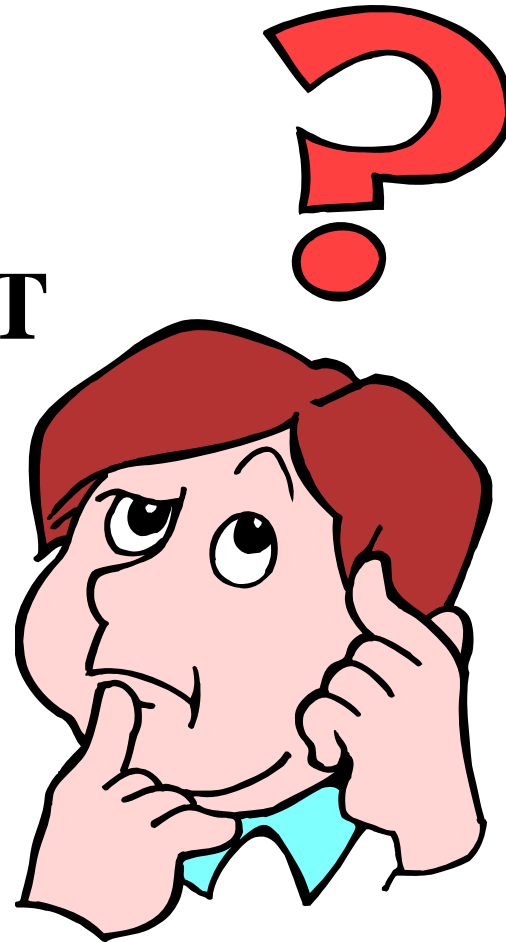
Labeling Sections are Difficult to Locate

The amount of intervening text **varies.**

Section locations occasionally **vary.**

This variability results in **wasted time and effort** looking for the critically needed drug information!

**WHY CHANGE
THE DRUG LISTING
AND ESTABLISHMENT
REGISTRATION
PROCESS THAT HAS
WORKED FOR
DECADES ????**



This is a detailed regulatory form, possibly an FDA submission form. It contains numerous sections with checkboxes and text entry fields. The form is organized into a structured layout with various headings and sub-sections, typical of official government documentation.

This form features a large grid or table structure, likely for data entry or tracking. It has multiple columns and rows, with some sections containing text and others containing numerical or categorical data. The grid is used for organizing and recording information systematically.

This form also features a grid structure, similar to the one above, but with more text and possibly different data fields. It appears to be another version or a related form, used for similar purposes of data entry and tracking. The layout is consistent with the other forms shown, suggesting they are part of the same regulatory process.

- Eliminate duplicative and redundant data entry
- Eliminate paper submissions
- Automate processing of data in a submission type in electronic format in a manner that FDA can adequately process, review, and archive.

Structured Product Labeling

The Structured Product Labeling (SPL) is a document markup standard approved by Health Level Seven (HL7) and adopted by FDA as a mechanism for exchanging product information.

SPL's Goal is to make the labels and drug listing information:

- **People friendly**
 - Labeling content in electronic format
 - Improve readability
 - Better access
- **Computer friendly**
 - Product information that is **computer readable**
 - Structured labeling content and product listing elements - Computer can “find” a specific section of the labeling and specific elements within labeling and product listing sections.
- **Information system friendly**
 - Product information in computer readable form - Easily imported into information systems
 - FDA systems extract the coded data from the SPL file to accomplish drug establishment registration and drug product listing
- **Publicly available**
 - Content of Labeling (up-to-date version) is made available by the FDA thru NLM (DailyMed) to consumers and health information suppliers
 - Drug listing and establishment registration information is made available by the FDA via NDC Directory, Drug Firms Annual Registration, and future FACTS@FDA websites.

XML & XSL Stylesheet

- SPL is created using **EX**tensible **M**arkup **L**anguage (XML) – similar to HTML for webpages
- XML
 - Relatively human-legible
 - Machine readable
 - Tags (elements) permit search of key information
- XML Documents – created via Notepad, Word Pad, XML editing tools, SPL authoring tools, SPL conversion services, Xforms, etc...
- XSL Stylesheet – transforms the XML data to be viewed via web browser or printed documents

SPL Stylesheet View/Source Code

CONTRAINDICATIONS

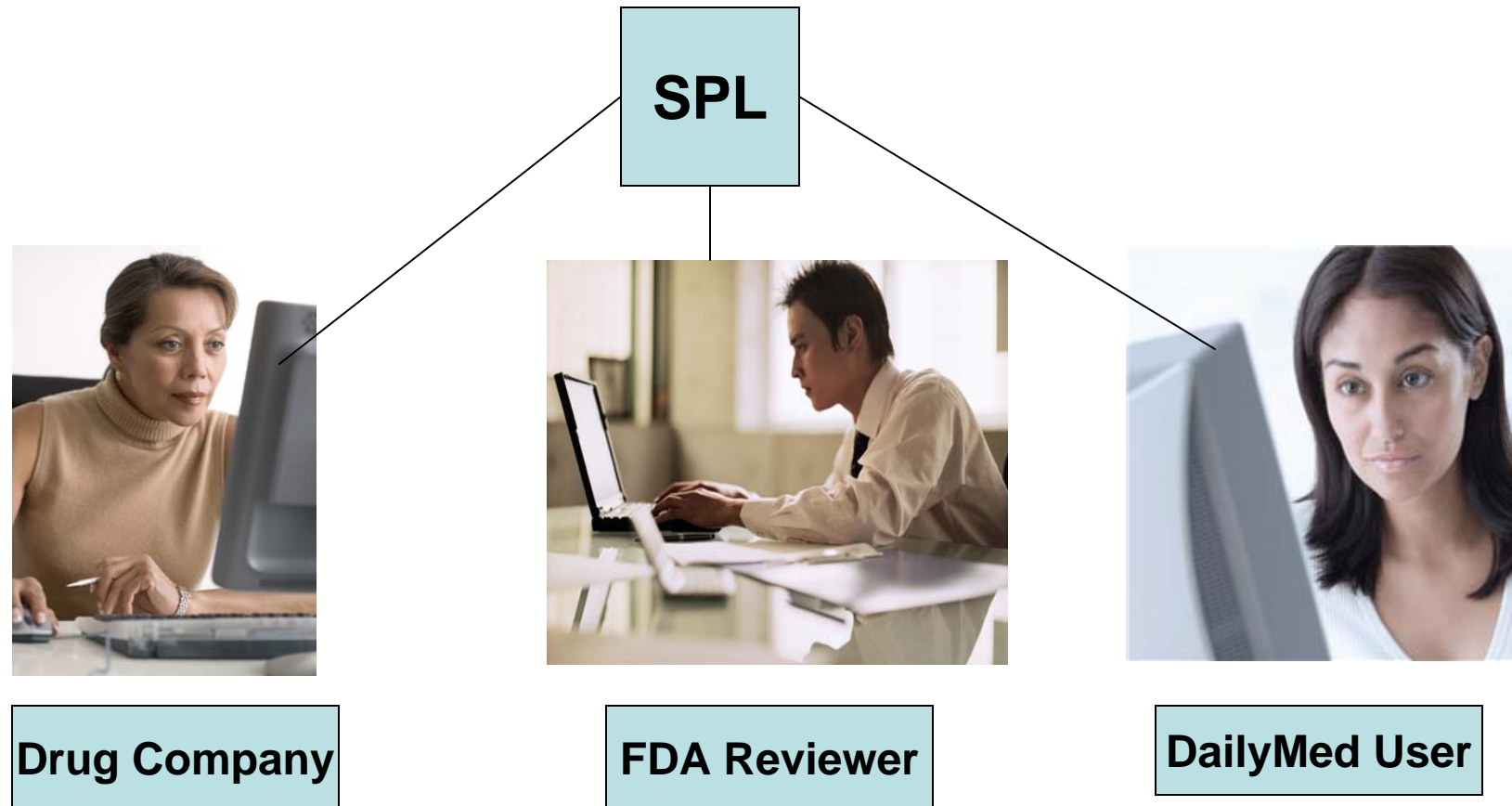
Miracle Drug Injection is contraindicated in severe toxic central nervous system depression or comatose states from any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.

```
<component>
<section ID="_7CF4D228-65A6-6223-5A96-ECB4DBD620FC">
<id root="3A7D815A-A2B9-0389-5D92-4836E709B0FE" />
<code code="34070-3" codeSystem="2.16.840.1.113883.6.1" displayName="CONTRAINDICATIONS SECTION" />
<title mediaType="text/x-hl7-title+xml">CONTRAINDICATIONS</title>
<text><paragraph>Miracle Drug Injection is contraindicated in severe toxic central nervous system depression or comatose states from
any cause and in individuals who are hypersensitive to this drug or have Parkinson's disease.</paragraph></text>
<effectiveTime value="20070813" />
</section>
```

SPL - Language

- XML is a “language” that computers or systems can “understand”
- SPL – the “alphabet” (Only certain XML elements can be used.)
- SPL document is a “**message**” that is used to exchange or communicate product information (SPL content)
- Drug company
 - Creates SPL using SPL standard to communicate product information.
 - Submits SPL to FDA
- FDA
 - Processes and validates SPL document using SPL standard
 - Transmits SPL to public repository (DailyMed/FACTS@FDA)
- DailyMed/FACTS@FDA/Health Information Supplier
 - Imports SPL into their system that uses the SPL standard
 - Displays and uses SPL data (label, listing data elements, etc..)

Information Exchange SPL



SPL is a standard that is used by drug companies, FDA and public to exchange or review or view product information. All three entities use computer or systems that “understand” SPL

SPL Authoring Options

- SPL authoring tools helps you “write” SPL documents using the XML language.
- Tools to translate your data into the XML language.
- SPL conversion vendors – provide a conversion service
- SPL Authoring/Document Management Tools – to integrate processing SPL into your IT environment
- XForms - Tool to create SPL content of labeling documents and the future eList & eReg SPL documents. (similar to Word processing software) (used as a training tool)

Implementation of SPL

- Electronic Labeling Rule (ELR) (final) – effective June 2004
- Docket 92S-0251 memorandum – September 2004
 - CDER's readiness to accept content of labeling in PDF or XML format
- Content of Labeling guidance document (final) April 2005
- Docket 92S-0251 memorandum – October 2005
 - Eliminated use of PDF as the acceptable format of electronic Content of Labeling – only acceptable format is HL7 Structured Product Labeling XML standard
- Physician Labeling Rule (final) – effective June 2006
- Public Availability of Labeling Changes in "Changes Being Effected" Supplements (draft) – September 2006
- Indexing SPL guidance document (final) – June 2008
- Guidance for Industry: Providing Regulatory Submissions in Electronic Format – Drug Establishment Registration and Drug Listing (Draft) – July 2008
- SPL Docket 92S-0251 - Drug Establishment Registration and Drug Listing – July 2008

Transitioning from Paper to Electronic Drug Establishment Registration & Drug Listing

Transition from Paper to Electronic Drug Establishment Registration & Drug Listing

- Changes in FD&C Act require electronic registration of drug establishments and listing of human prescription drugs, OTC, animal drug, biologic products – September 2007
- Draft Guidance document for electronic drug establishment registration and listing – July 2008
- FDA is adopting the use of extensible markup language (XML) files in SPL format as the standard format for the exchange of drug establishment registration and drug listing information.

Benefits of Electronic Registration and Listing

- Electronic registration and listing process is more efficient and effective for industry and the Agency
- Accurate, up-to-date inventory of marketed drugs
- Eliminates data entry errors
- Well formed and properly created SPL files can be processed in minutes
- Use existing technology and data standard – **SPL (Used by FDA (CDER) since 2004)(Required by CDER in 2005)**
- Standard was updated to SPL R4 to include data elements needed to register drug establishments and list drug products

More Benefits of Electronic Registration and Listing

- Data maintenance
 - Content of Labeling and listing information in one file.
 - Registrant can list all it's establishments in one file.
 - Update information – Use one file instead of creating several paper forms and resubmit.
- Eliminates the use of paper forms for listing and registration
- 24-hour submission window – FDA Gateway
- Manage data using same source (files) as FDA
- Reduces the amount of time for FDA to receive and process your information.

Paper Listing Review



Electronic Listing Review



Terminology

- Only controlled terminology is permitted in SPL documents
- Terminology Resources
 - National Cancer Institute Thesaurus
 - FDA Data Standards Council's SPL web page (acceptable terms for use in SPL documents):
<http://www.fda.gov/oc/datacouncil/spl.html>

Transitioning from Paper to Electronic: Drug Registration and Listing

- If you electronically list your product(s) do not list the same product(s) using paper (FDA Form 2657 or FDA Form 2658)
- If you register your drug establishment(s) electronically, do not register the same drug establishment(s) using the paper (FDA Form 2656)

(2656, 2657, 2658) with...

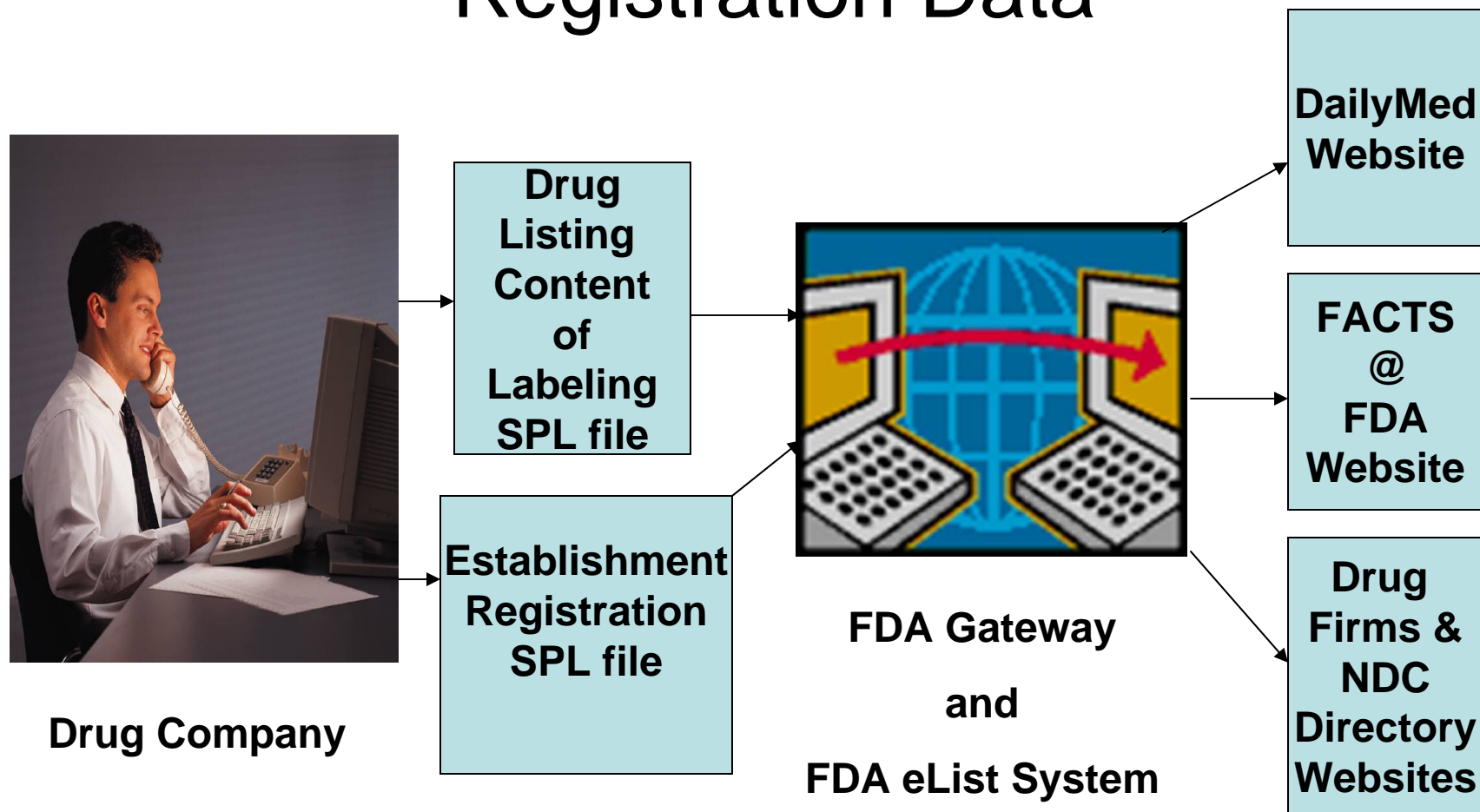
Save As... <small>(Click here)</small>	Print Page <small>(Click here)</small>	Print Form <small>(Click here)</small>	
Form Approved - CME No. 0910-046; Expiration Date: December 31, 2007		See ONE Statement on Reverse	
FDA USE ONLY DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION REGISTRATION OF DRUG ESTABLISHMENT/ LABELER CODE ASSIGNMENT <small>(in accordance with Public Law 102-227)</small>		FDA USE ONLY	
NOTICE: This report is required by law [21 C.F.R. 312.25]. Failure to report can result in imprisonment for not more than one year or a fine of \$100,000 or both. (21CFR312.25) Expiry: 2007		LABELER CODE	REGISTRATION NUMBER
SECTION A - SITE INFORMATION REPORTING FIRM NAME:		STATE OF INC.	
SITE ADDRESS (No R.O. Box)		SITE TELEPHONE NUMBER ()	
CITY	STATE <input type="text"/> ZIP CODE COUNTRY	BUSINESS CATEGORY: <input type="checkbox"/> HUMAN <input type="checkbox"/> VETERINARY	
SITE MAILING ADDRESS (if different from above address)			
CITY	STATE <input type="text"/> ZIP CODE COUNTRY	SITE INTERNET/ELECTRONIC ADDRESS	
DOING BUSINESS AS (DBA) NAME OF FIRM (if applicable)			
PARENT COMPANY NAME			
REASON(S) FOR SUBMISSION		TYPICAL TYPE OF OWNERSHIP	
<input type="checkbox"/> Firm Registration	<input type="checkbox"/> Address Change	<input type="checkbox"/> Sole Proprietorship	
<input type="checkbox"/> Registration of Additional Site	<input type="checkbox"/> Mergers/acq.	<input type="checkbox"/> Partnership	
<input type="checkbox"/> Re-registration	<input type="checkbox"/> New/Existing Business acq./Trans. Name	<input type="checkbox"/> Corp. Acqn.	
<input type="checkbox"/> LQ Assignment	<input type="checkbox"/> Initial Closure	<input type="checkbox"/> Corporation	
		<input type="checkbox"/> Other _____	
SECTION B - FIRM COMPLIANCE MAILING ADDRESS (For Annual, Warning Letters and/or Penalties Correspondence)		PURSUANT TO THE DATA AND TELEPHONE	
NUMBER AND STREET AND/OR P.O. BOX AND ATTENTION LINE AND/or Internal Mail Code		BUSINESS TYPE	
CITY		<input type="checkbox"/> Distributor*	
STATE <input type="text"/> ZIP CODE COUNTRY		<input type="checkbox"/> Foreign Country	
		<input type="checkbox"/> Manufacturer	
		<input type="checkbox"/> Importer	
		<input type="checkbox"/> Analytical Lab	
		<input type="checkbox"/> Supplier	
		COMPLIANCE INTERNET/ELECTRONIC ADDRESS	
SECTION C - ADDITIONAL FIRM AND SITE INFORMATION			
NAME OF OWNER, PARTNER, OR OFFICER		TITLE	
OTHER FIRMS DOING BUSINESS AT THIS SITE			
LABELER CODE	FIRM NAME	LABELER CODE	FIRM NAME
SECTION D - SIGNATURE			
SIGNATURE OF AUTHORIZING OFFICIAL		DATE	
* DISTRIBUTORS CERTIFICATION: As a Distributor, I am submitting product listing information to the FDA on my own behalf. I have provided a copy of this certification (FDA USE) to the registered manufacturer(s). My signature and office number are listed below.			
RETURN THIS FORM TO: FOOD AND DRUG ADMINISTRATION CDER/OS REGISTRATION AND LISTING (HFD-32) 5600 Fishers Lane Rockville, MD 20857 TDD/TELETYPE: CDER/OPHA HAS 520V		SIGNATURE OF DISTRIBUTOR	
		DISTRIBUTOR'S TELEPHONE NUMBER ()	
FORM FDA 243e (06/07) (PHOT)			

[illegible][illegible]

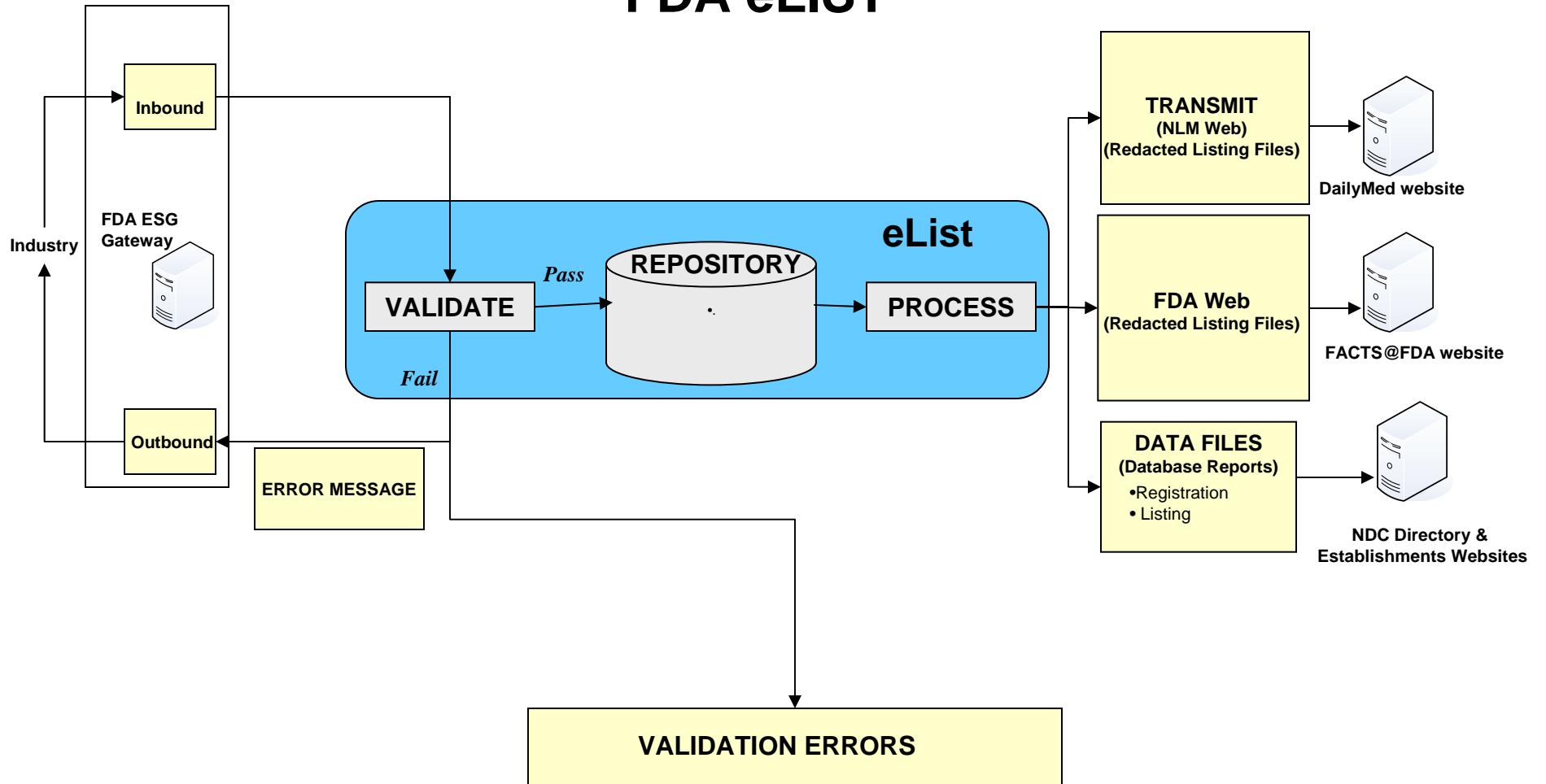
...three e-Files for Registration & Listing – SPL Format

- NDC Labeler Code Request
- Establishment Registration
- Content of labeling (CoL)/Listing

You Control the Published Electronic Drug Listing and Establishment Registration Data



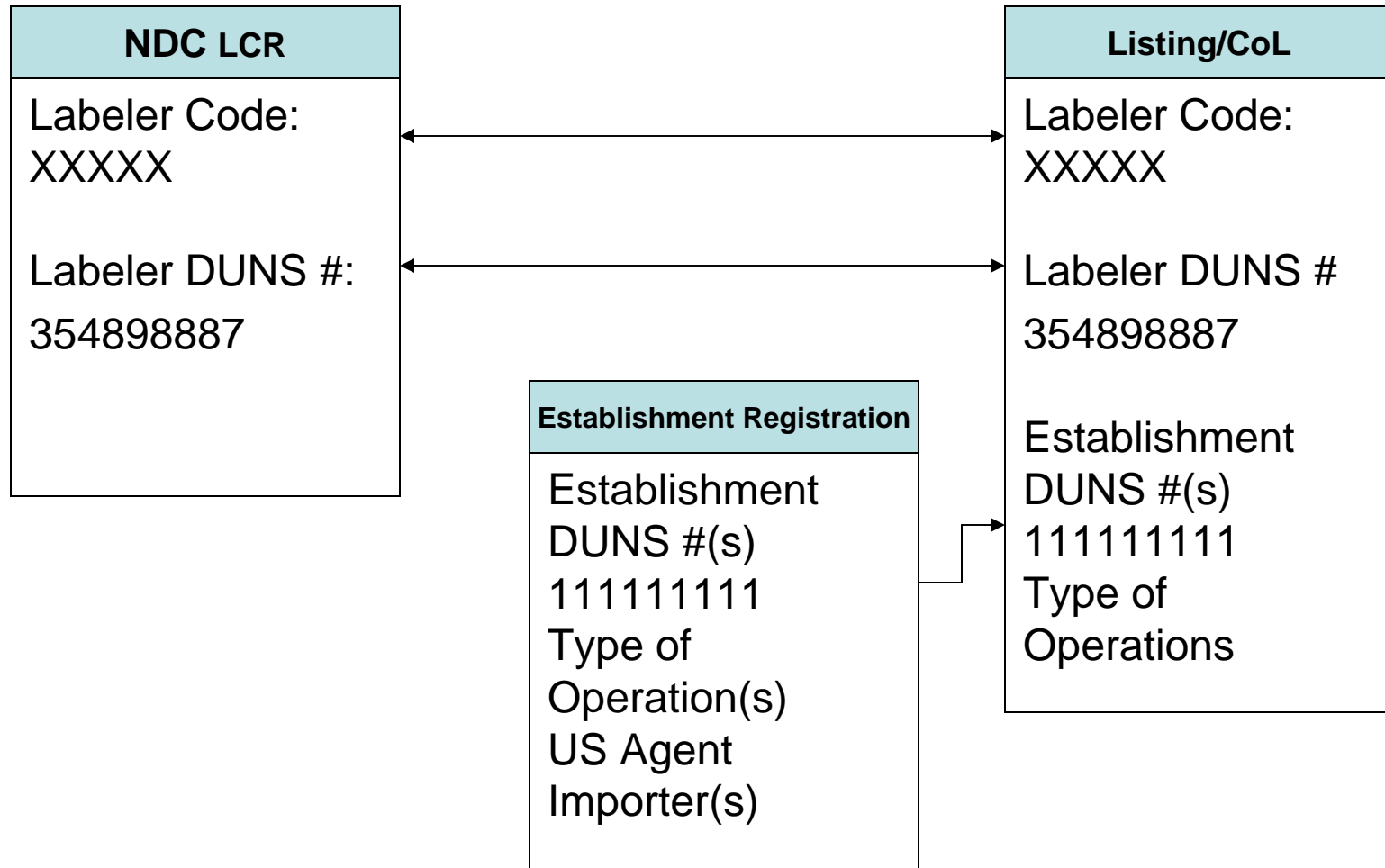
FDA eLIST



Order of Submissions

1. NDC Labeler Request (LCR) and Establishment Registration (ER) SPL
 2. CoL/Listing SPL
- CoL/Listing validates against data submitted in NDC LCR and ER SPL

Data Source – SPL Documents



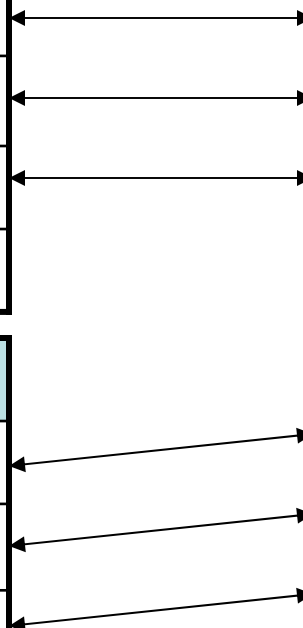
eList Data Relationships

Mockup

NDC LCR Table
Labeler Name
Labeler DUNS #
Labeler Code
SetID

Establishment Table
Establishment Name(s)
Establishment DUNS #(s)
Type of Operation(s)
US Agent
Importer
SetID

Listing Table
Labeler Name
Labeler DUNS #
Labeler Code
NDC Product Code
NDC Package Code
Establishment Name(s)
Establishment DUNS #(s)
Type of Operation(s)
SetID



Query Example Mockup

FDA eList System

Listed Product Verification

Establishment Search	NDC Package Code: XXXXX-XXX-X
	Establishment DUNS #111111111

Listing Database Table	
Field Name	Field Value
Labeler Name	Jaysonian Pharm
Labeler DUNS #	354898887
Labeler Code	XXXXX
NDC Product Code	XXXXX-XXX
NDC Package Code	XXXXX-XXX-X
Establishment Name(s)	Pham Pharma
Establishment DUNS #(s)	111111111
Type of Operation(s)	Manufacture
SetID	027005a5-4c40-4931-85cd-79933f99e338

Product Package

**Miracle Drug XR
(good drug) Tablets**

30 Tablets
NDC: XXXXX-XXXX-X
DUNS #111111111

Important: not a depiction of FDA's System – for demo only

Using the SPL Format to Electronically Register Drug Establishments and List Drug Products

Document Tracking Information

Basic information to identify the SPL document:

- **Document ID:** is a Globally Unique Identifier (GUID) and is unique for each version of the document. Letters used in a GUID are lower case.
- **Document Type:** The <code> is the LOINC code which provides information on the document type.
- **Effective Time:** provides a date reference to the SPL version including the year, month and day as yyyyymmdd.
- **SetID:** is a GUID and is a unique identifier for the document that remains constant through all versions/revisions of the document.
- **Version number:** is an integer greater than zero that provides a sequence to the versions of the document.

NDC Labeler Code Request

NDC Labeler Code Request Data

- **Document Information**

- Type of document
- ID
- Set ID
- Version Number
- Effective Time

- **Labeler**

- Name
- DUNS Number
- NDC Labeler Code

- **Contact**

- Name
- Mailing Address
- City
- State
- Country
- Postal Code
- Telephone Number
- Email Address

NDC Labeler Code Request Xforms View

HL7 SPL - NDC Labeler Code Request v 0.71	
<div>Open Save As Save</div>	
<div>NDC Labeler Code Request Preview</div>	
Document Information	
Type of document	NDC LABELER CODE REQUEST
ID	3267a844-378f-4020-912b-43babb77001d
Set ID	8d24aab5-8f91-42ca-9637-997a3d223e5c
Version Number	1
Effective Time	20080909
example(YYYYMMDD)	
Labeler	
Name	Acme Pharmaceuticals, Inc
DUNS Number	111119999
NDC Labeler Code	44444
<div>Add NDC Labeler Code Delete NDC Labeler Code</div>	
Contact	
Name	Charles Daniels
Mailing Address	44 Pembroke Drive
City	Rockville
State	MD
Country	USA
Postal Code	20888
Telephone Number	tel:+1-888-888-4757
Email Address	mailto:charles.daniels@acme-pharmaceuticals
example(tel:+1-201-555-1212) example(mailto:xportal@globalsubmit.com)	

NDC Labeler Code Request SPL Document

Acme Pharmaceuticals, Inc

Product Information	
Product Type	NDC LABELER CODE REQUEST

Labeler - Acme Pharmaceuticals, Inc (111119999) **NDC Labeler Code:** 44444

Contact	Address	Telephone Number	Email Address
Charles Daniels	Address: 44 Pembroke Drive City, State, Zip: Rockville , MD, 20888 Country: USA	+1-888-888-4757	charles.daniels@acme-pharmaceuticals.com

Revised: 09/2008

Acme Pharmaceuticals, Inc

NDC LCR SPL Scenarios

- **Requesting a new NDC Labeler Code**
 - Fill out the *NDC Labeler Code request* as described in sections 2.1 through 2.4 leaving the NDC Labeler Code field empty.
 - Requests for NDC Labeler Codes are individually evaluated prior to entry into the NDC System. The initial request will be automatically stopped because there is no NDC Labeler Code provided and is diverted to a FDA reviewer. Once the evaluation is completed, the response to the request is directed to the designated contact person.
 - Once the NDC Labeler Code is assigned, open the original SPL file and add the newly assigned NDC Labeler Code and resubmit the corrected file.
- **Initial electronic submission when NDC Labeler Code already assigned**
 - Fill out the *NDC Labeler Code request*. Only one NDC Labeler Code is included in an SPL file. In other words, use a different setId root for each NDC Labeler Code request.

NDC LCR SPL

Scenarios cont...

- **Correct SPL file validation error**
 - If an SPL file cannot be processed because of a validation error, a report on the validation error is sent from FDA to the contact person. Open the SPL file and correct the errors.
- **Correct a mistake in an SPL file just submitted**
 - Open the SPL file, correct the mistake, and fill in a **new id root** and **new version number** with the **original setId root** and the appropriate effective time.

NDC LCR SPL

Scenarios cont...

- **Update the NDC Labeler Code information**
 - Open the previous SPL file and fill in the new information without changing the other existing information. Fill in a **new id root** and **new version number** with the **original setld root** and the appropriate effective time.
- **Requesting a second NDC Labeler Code**
 - Only one NDC Labeler Code is associated with each *NDC Labeler Code request*. If a second NDC Labeler Code is requested, fill out a separate SPL file with a **different setld root**. The labeler information and contact information is the same as the SPL file for the first NDC Labeler Code request

Establishment Registration

Establishment Registration Data

- **Document Information**

- Type of Document
- ID
- Set ID
- Version Number
- Effective Time

- **Registrant**

- Name
- DUNS Number

- **Registrant Contact**

- Name
- Mailing Address
- City
- State
- Country
- Postal Code
- Telephone Number
- Email Address

Establishment Registration Data (cont...)

- **Establishment**
 - Name
 - DUNS Number
 - FEI
 - Street Address
 - City
 - State
 - Country
 - Postal Code
 - Type of Operation(s)
- **Establishment Contact**
 - Name
 - Mailing Address
 - City
 - State
 - Country
 - Postal Code
 - Telephone Number
 - Email Address

Establishment Registration Data (cont...)

- **US Agent (if applicable)**
 - Name
 - DUNS number
 - Telephone Number
 - Email Address
- **Importer (if applicable)**
 - Name
 - DUNS number
 - Telephone Number
 - Email Address

Establishment Registration

SPL Xforms

HL7 SPL - Establishment Registration v 0.71	
<div>Open Save As Save</div>	
<div>Establishment Registration Preview</div>	
Document Information	
Type of Document	ESTABLISHMENT REGISTRATION
ID	4ff69f20-6dc3-49ca-bb3c-0d589ff4c0b1
Set ID	118ec196-50d7-49b2-946a-831d29702818
Version Number	1
Effective Time	20080909
example(YYYYMMDD)	
Registrant	
Name	Acme, Inc.
DUNS Number	2223334441
Registrant Contact	
Name	Deborah Tyler
Mailing Address	222 Bonifant Avenue
City	Fort Washington
State	PA
Country	USA
Postal Code	35295
Telephone Number	tel:+1-800-435-4585
Email Address	mailto:deborah.tyler@acme.com
example(tel:+1-201-555-1212) example(mailto:xportal@globalsubmit.com)	

Establishment Registration

SPL Xforms cont...

Establishment		
Name	Acme Manufacturing, Inc.	
DUNS Number	475859252	
FEI	35295835928	
<input type="button" value="Add FEI"/> <input type="button" value="Delete FEI"/>		
Street Address	777 Sampson Street	
City	Mason	
State	PA	
Country	USA	
Postal Code	35859	
Type of Operation	manufacture ▼	
<input type="button" value="Add Type of Operation"/> <input type="button" value="Delete Type of Operation"/>		
Establishment Contact		
Name	Pam Jamison	
Mailing Address	777 Sampson Street	
City	Mason	
State	PA	
Country	USA	
Postal Code	35859	
Telephone Number	tel:+1-800-778-8359	example(tel:+1-201-555-1212)
Email Address	mailto:pam.jamison@acme.com	example(mailto:xportal@globalsubmit.com)
<input type="button" value="Add US Agent"/> <input type="button" value="Delete US Agent"/>		
<input type="button" value="Add Importer"/> <input type="button" value="Delete Importer"/>		

Establishment Registration

SPL Xforms cont...

Establishment	
Name	Acme International
DUNS Number	98583572
FEI	25835925829
<input type="button" value="Add FEI"/> <input type="button" value="Delete FEI"/>	
Street Address	33 Bleu Rue
City	Paris
State	
Country	FRA
Postal Code	20583
Type of Operation	manufacture
Type of Operation	analysis
<input type="button" value="Add Type of Operation"/> <input type="button" value="Delete Type of Operation"/>	
Establishment Contact	
Name	Etienne St. Champs
Mailing Address	33 Bleu Rue
City	Paris
State	
Country	FRA
Postal Code	20583
Telephone Number	tel:+33-538-5859
Email Address	mailto:etienne.st-champs@acme.com

example(tel:+1-201-555-1212)
example(mailto:xportal@globalsubmit.com)

Establishment Registration

SPL Xforms cont...

Establishment Contact		
Name	Etienne St. Champs	
Mailing Address	33 Bleu Rue	
City	Paris	
State		
Country	FRA	
Postal Code	20583	
Telephone Number	tel:+33-538-5859	example(tel:+1-201-555-1212)
Email Address	mailto:etienne.st-champs@acme.com	example(mailto:xportal@globalsubmit.com)
US Agent		
Name	Acme USA	
DUNS number	359582424	
Telephone Number	tel:+1-800-999-5542	example(tel:+1-201-555-1212)
Email Address	mailto:jacob.goodman@acme.com	example(mailto:xportal@globalsubmit.com)
<input type="button" value="Add US Agent"/> <input type="button" value="Delete US Agent"/>		
Importer		
Name	Franklin Imports	
DUNS number	252597793	
Telephone Number	tel:+1-888-444-5835	example(tel:+1-201-555-1212)
Email Address	mailto:paula.johansen@franklin.com	example(mailto:xportal@globalsubmit.com)
<input type="button" value="Add Importer"/> <input type="button" value="Delete Importer"/>		
<input type="button" value="Add Establishment"/> <input type="button" value="Delete Establishment"/>		

Establishment Registration SPL Document

Product Information	
Product Type	ESTABLISHMENT REGISTRATION

Registrant - Acme, Inc. (2223334441)			
Contact	Address	Telephone Number	Email Address
Deborah Tyler	Address: 222 Bonifant Avenue City, State, Zip: Fort Washington, PA, 35295 Country: USA	+1-800-435-4585	deborah.tyler@acme.com

Establishment			
Name	Address	ID/FEI	Operations
Acme Manufacturing, Inc.	Address: 777 Sampson Street City, State, Zip: Mason, PA, 35859 Country: USA	475859252	manufacture
Contact	Address	Telephone Number	Email Address
Pam Jamison	Address: 777 Sampson Street City, State, Zip: Mason, PA, 35859 Country: USA	+1-800-778-8359	pam.jamison@acme.com

Establishment Registration

SPL Document cont...

	Country: FRA		
Establishment			
Name	Address	ID/FEI	Operations
Acme International	Address: 33 Bleu Rue City, State, Zip: Paris, 20583 Country: FRA	98583572	manufacture, analysis
Contact	Address	Telephone Number	Email Address
Etienne St. Champs	Address: 33 Bleu Rue City, State, Zip: Paris, 20583 Country: FRA	+33-538-5859	etienne.st-champs@acme.com
US Agent (ID)	Address	Telephone Number	Email Address
Acme USA (359582424)		+1-800-999-5542	jacob.goodman@acme.com
Importer (ID)	Address	Telephone Number	Email Address
Franklin Imports (252597793)		+1-888-444-5835	paula.johansen@franklin.com

Revised: 09/2008

Establishment Registration Scenarios

- **Initial electronic submission for establishments already registered**
 - Registrants include information for all of their establishments in one *Establishment Registration* SPL file. Each establishment is in only one SPL file.
- **Correct SPL file validation error**
 - If an SPL file cannot be processed because of a validation error, a report on the validation error is sent from FDA to the contact person. Open the SPL file and correct the errors.

Establishment Registration Scenarios cont...

- **Correct a mistake in an SPL file just submitted**
 - Open the SPL file, correct the mistake, and fill in a **new id root** and **new version number** with the **original setld root** and the appropriate effective time.
- **Update information for a registered establishment**
 - Open the previous SPL file and fill in the new information without changing the other existing information. Fill in a **new id root** and **new version number** with the **original setld root** and the appropriate effective time.

Establishment Registration

Scenarios cont...

- **Add a new establishment**
 - Open the previous SPL file and fill in the information on a new establishment without changing the information on the other establishments. Fill in a **new** id root and **new** version number with the **original** setId root and the appropriate effective time.
- **Remove a previously registered establishment**
 - Open the previous SPL file, without changing the existing information on the other establishments, and remove the specific establishment information. Fill in a **new** id root and **new** version number with the **original** setId. At the next update,

Establishment Registration

Scenarios cont...

- **No changes to registration information**
 - Each year when the information is updated, if there is no change, create an SPL file with the *document type* **No change notification** with a **new** id root and **new** version number with the **original** setId and the appropriate effective time. Registrant and establishment information is not included with an SPL file with the *document type* **No change notification**.
- **Registrant goes out of business**
 - If the registrant goes out of business, create an SPL file with the *document type* **Out of business notification** using a **new** id root and **new** version number with the **original** setId and the appropriate effective time. Registrant and establishment information is not included with an SPL file with the *document type* **Out of business notification**.

Content of Labeling/Listing

Content of Labeling/Listing Data

- **Document Information**
 - Type of document
 - ID
 - Set ID
 - Version Number
 - Effective Time

Content of Labeling/Listing Data cont...

- **Drug Listing**
- **Labeler**
 - Name
 - DUNS Number
- **Registrant**
 - Name
 - DUNS number
 - Mark as Confidential
- **Establishment**
 - Name
 - DUNS number
 - Mark as Confidential
 - Type of operation
 - Product
 - ID (section ID)
 - Effective Time

Content of Labeling/Listing Data cont...

- **Product Information**
 - Proprietary Name
 - Proprietary Name Suffix
 - Non-Proprietary Name
 - NDC Product Code
 - Dosage Form
 - Source NDC Product Code (if applicable)
 - DEA Schedule (if applicable)
 - Route(s) of Administration
- **Active Ingredient**
 - Name(s)
 - Unique Ingredient Identifier(s) (UNII)
 - Strength
- **Reference Drug**
 - Name
 - Unique Ingredient Identifier (UNII)

Content of Labeling/Listing Data cont...

- **Active Moiety**
 - Name(s)
 - Unique Ingredient Identifier(s) (UNII)
 - Basis of Strength
- **Inactive Ingredient**
 - Name(s)
 - Unique Ingredient Identifier(s) (UNII)
 - Mark as Confidential
 - Strength
- **Flavor**
 - Name(s)
 - Original Text

Content of Labeling/Listing Data cont...

- **Imprint Information**
 - Color(s)
 - Original Text
 - Score
 - Shape
 - Original Text
 - Imprint Code
 - Size
 - Size Unit

Content of Labeling/Listing Data cont...

- **Marketing Date**
 - Product Status
 - Start Marketing Date
 - End Marketing Date (if applicable)
- **Marketing Category**
 - Marketing Category
 - Application or citation number
 - Application or citation number code system

Content of Labeling/Listing Data cont...

- **Packaging**
 - **Immediate packaging**
 - NDC Package Code (10 digit)
 - Quantity
 - Package Type
 - **Outer package**
 - NDC Package Code (10 digit)
 - Quantity
 - Package Type

Content of Labeling/Listing Data cont...

- **Product Parts**
 - Proprietary Name
 - Proprietary Name Suffix
 - Non-Proprietary Name
 - NDC Product Code
 - Dosage Form
 - Total Product Quantity
 - Source NDC Product Code (if applicable)
 - DEA Schedule (if applicable)
 - Route(s) of Administration

Content of Labeling/Listing cont...

- **Active Ingredient**
 - Name(s)
 - Unique Ingredient Identifier(s) (UNII)
 - Strength
- **Reference Drug**
 - Name
 - Unique Ingredient Identifier (UNII)
- **Active Moiety**
 - Name(s)
 - Unique Ingredient Identifier(s) (UNII)
 - Basis of Strength

Content of Labeling/Listing Data cont...

- **Inactive Ingredient**
 - Name(s)
 - Unique Ingredient Identifier(s) (UNII)
 - Mark as Confidential
 - Strength
- **Flavor**
 - Name(s)
 - Original Text
- **Imprint Information**
 - Color(s)
 - Original Text
 - Score
 - Shape
 - Original Text
 - Imprint Code
 - Size
 - Size Unit

Content of Labeling/Listing Data cont...

- **Marketing Date**
 - Product Status
 - Start Marketing Date
 - End Marketing Date (if applicable)
- **Marketing Category**
 - Marketing Category
 - Application or citation number
 - Application or citation number code system

Content of Labeling/Listing Data cont...

- **SPL Product Image** (location in slide is not indicative of placement in SPL)
- **Packaging**
 - **Immediate packaging**
 - NDC Package Code (10 digit)
 - Quantity
 - Package Type
 - **Outer package**
 - NDC Package Code (10 digit)
 - Quantity
 - Package Type

Drug Listing/CoL SPL Xforms

HL7 SPL - Drug Listing v 0.71	
<div>Open Save As Save</div>	
<div>Document Information Drug Listing Content of Labeling Preview</div>	
Document Information	
Type of document	<div>HUMAN PRESCRIPTION DRUG LABEL</div>
ID	<div>8c561834-cee2-4731-b9b9-cd9db64c030d</div>
Set ID	<div>11342435-a415-415a-81b6-d68d23b90b83</div>
Version Number	<div>1</div>
Effective Time	<div>20090909</div> <div>example(YYYYMMDD)</div>

Drug Listing/CoL SPL Xforms cont...

HL7 SPL - Drug Listing v 0.71	
<div>Open Save As Save</div>	
<div>Document Information Drug Listing Content of Labeling Preview</div>	
Labeler	
Name	Acme Pharmaceuticals, Inc
DUNS Number	111119999
Registrant	
Name	
DUNS number	
Mark as Confidential	<input type="checkbox"/>
Establishment	
Name	Acme Manufacturing, Inc.
DUNS number	475859252
Mark as Confidential	<input type="checkbox"/>
Type of operation	manufacture
<div>Add Type of Operation Delete Type of Operation</div>	
Establishment	
Name	Acme International
DUNS number	98583572
Mark as Confidential	<input type="checkbox"/>
Type of operation	manufacture
Type of operation	analysis
<div>Add Type of Operation Delete Type of Operation</div>	
<div>Add Establishment Delete Establishment</div>	

Drug Listing/CoL SPL Xforms cont...

ID	82df6f14-84c2-4d98-9551-fb4f4527e921	
Effective Time	20090909	example(YYYYMMDD)

Product Information

Proprietary Name	Miracle
Proprietary Name Suffix	XR
Non-Proprietary Name	Good Drug
NDC Product Code	44444-333
Dosage Form	TABLET

DEA Schedule	CII
--------------	-----

Route of Administration	ORAL
-------------------------	------

Active Ingredient

Name	Good Drug			
Unique Ingredient Identifier (UNII)	245895XFT			
Strength	25	mg	in	1

Active Moiety

Name	active moiety
Unique Ingredient Identifier (UNII)	538TW3529

Basis of Strength	Active Ingredient
-------------------	-------------------

Drug Listing/CoL

SPL Xforms cont...

Inactive Ingredient	
Name	<input type="text" value="Inactive ingredient one"/>
Unique Ingredient Identifier (UNII)	<input type="text" value="X5385925T3"/>
Mark as Confidential	<input checked="" type="checkbox"/>
<input type="button" value="Add Strength"/>	<input type="button" value="Delete Strength"/>
<input type="button" value="Add Inactive Ingredient"/> <input type="button" value="Delete Inactive Ingredient"/>	
Flavor	
Name	<input type="text" value="CITRUS"/>
Original Text	<input type="text" value="citrus-flavored"/>
<input type="button" value="Add Flavor"/>	<input type="button" value="Delete Flavor"/>
Imprint Information	
Color	<input type="text" value="yellow"/>
Original Text	<input type="text" value="yellow-orange"/>
<input type="button" value="Add Color"/>	<input type="button" value="Delete Color"/>
Score	<input type="text" value="Two even pieces"/>
Shape	<input type="text" value="ROUND"/>
Original Text	<input type="text" value="ROUND"/>
Imprint Code	<input type="text" value="AC;25;mg"/>
Size	<input type="text" value="18"/>
Size Unit	<input type="text" value="mm"/>
<input type="button" value="Add Imprint"/>	<input type="button" value="Delete Imprint"/>

Drug Listing/CoL

SPL Xforms cont...

Marketing Date	
Product Status	Active
Start Marketing Date	20070413
example(YYYYMMDD)	

Marketing Category	
Marketing Category	NDA
Application or citation number	NDA024380
Add Application or citation number	Delete Application or citation number
Application or citation number code system	Application
Add Application or citation number code system	Delete Application or citation number code system
Add Product image	Delete Product image

Packaging			
NDC Package Code (10 digit)	44444-333-50		
Quantity	50		
Package Type	TABLET		
NDC Package Code (10 digit)	44444-333-10		
Quantity	1		
Package Type	BOTTLE		
CARTON			
Add Package	Delete Package	Add Outer Package	Delete Outer Package

Product Parts	
Add Product Part	Delete Product Part
Add Product	Delete Product

Drug Listing/CoL SPL Xforms cont...

Open		Save As		Save	
Document Information		Drug Listing		Content of Labeling	
Content of Labeling					
Title		<input type="text" value="Miracle XR"/>			
Add Title		Delete Title			
Section		<input type="text" value="DESCRIPTION SECTION"/>			
Add Hyperlink ID		Delete Hyperlink ID			
ID		<input type="text" value="49f13953-fe26-475b-af74-d2f3b1ff2fea"/>			
Title		<input type="text" value="Description"/>			
Add Title		Delete Title			
Effective time		<input type="text" value="20070531"/>			
Add Effective time		Delete Effective time			
Add Highlight		Delete Highlight			
Section Text					
Description text placeholder					
Edit					
Observation Media					
Add Media		Delete Media			
Add Sub-Section		Delete Sub-Section			
Add Section		Delete Section			

Drug Listing/CoL SPL Document

MIRACLE XR - good drug tablet
Acme Pharmaceuticals, Inc

Miracle XR

Description

Description text placeholder

Drug Listing/CoL SPL Document

MIRACLE XR

good drug tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	NDC Product Code (Source)	44444-333
Route of Administration	ORAL	DEA Schedule	CII

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Good Drug (active moiety)	Good Drug	25 mg

Inactive Ingredients

Ingredient Name	Strength
Inactive ingredient one	

Product Characteristics

Color	yellow (yellow-orange)	Score	2 pieces
Shape	ROUND (ROUND)	Size	18mm
Flavor	CITRUS (citrus-flavored)	Imprint Code	AC;25;mg
Contains			

Packaging

#	NDC	Package Description	Multilevel Packaging
1	44444-333-10	1 BOTTLE In 1 CARTON	contains a BOTTLE (44444-333-50)
1	44444-333-50	50 TABLET In 1 BOTTLE	This package is contained within the CARTON (44444-333-10)

Drug Listing/CoL SPL Document

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA024380	04/13/2007	

Labeler - Acme Pharmaceuticals, Inc (111119999)

Establishment

Name	Address	ID/FEI	Operations
Acme Manufacturing, Inc.		475859252	manufacture

Establishment

Name	Address	ID/FEI	Operations
Acme International		98583572	manufacture, analysis

Establishment Information for Inactive Ingredient Manufacturers

- Establishment information for manufacturers of **inactive ingredients** in your products to be listed – does **NOT** need to be included in your **electronic drug listing SPL**.

Drug Listing Establishment Information for API Manufacturers

- Establishment information for manufacturers of your **active pharmaceutical ingredient (API)** used in your products – Recommendation that this information **should** be included in your **electronic drug listing document** (SPL file)
- Listing of API used by one company - Include the establishment for the API in the listing SPL file for the finished product. **This lists the API.**

Content of Labeling/Listing Scenarios

- **Initial listing submission when release 3 SPL file previously submitted**
 - Update the previous SPL release 3 file to an SPL release 4 file with the additional drug listing information and submit a new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.
- **Initial listing submission with drugs previously listed**
 - The drug listing information is provided in a single SPL file. More than one drug products are included in a single SPL file when the products relate to the same content of labeling. Each drug product is included in only one SPL file unless it is being repacked or relabeled. Note that drug listing includes all jpg files associated with the content of labeling. The drug listing SPL file is separate from the SPL file for NDC Labeler Code request and the SPL file for establishment registration.

Content of Labeling/Listing Scenarios cont...

- **Initial listing submission when the private label distributor provides the SPL file**
 - If the private label distributor chooses to provide the SPL file with the drug listing information, the private label distributor includes all of the information that would have been supplied by the registrant including all establishments involved in the manufacturing and processing of the drug product. The registrant does **not** submit a drug listing SPL file for this drug product. If the private label distributor chooses not to provide the SPL file with the drug listing information, then the registrant provides the SPL file.
- **Initial listing submission when the registrant provides the SPL file for a drug made for a private label distributor**
 - If the private label distributor chooses not to provide the SPL file with the drug listing information, then the registrant provides the SPL file. The registrant includes the name of the private label distributor as the labeler, itself as the registrant, and all establishments involved in the manufacturing and processing of the drug.

Content of Labeling/Listing

Scenarios cont...

- **Initial listing submission with more than one registrant involved**
 - When more than one registrant is involved in manufacturing and processing a single drug product (e.g., contract manufacturers), only one registrant provides the SPL file with the drug listing information for the drug product. The registrant who provides the SPL file includes, in addition to its own establishments, all establishments of the other registrants involved in the manufacturing and processing of the drug product.
- **Initial listing submission for bulk ingredients**
 - The registrant provides the SPL file with the drug listing information for the bulk drug ingredients (e.g., active pharmaceutical ingredient).

Content of Labeling/Listing Scenarios cont...

- **Initial listing submission for a registrant using a marketed bulk ingredient**
 - The registrant provides the SPL file with the drug listing information for its drug product. The registrant includes the NDC Product Code for the marketed bulk drug ingredient as the source NDC or the establishments used in manufacturing or processing the bulk ingredient.
- **Initial listing submission for a registrant repacking or relabeling a marketed drug product**
 - The repacker or relabeler provides the SPL file with the drug listing information for its drug product including the NDC Product Code for the source marketed drug product.

Content of Labeling/Listing Scenarios cont...

- **Initial listing submission for a kit including two or more drug products**
 - The registrant or private label distributor provides the SPL file with the drug listing information for its kit. The SPL file also includes drug listing information for each drug product in the kit (component) including NDC Product Codes and NDC Package Codes, if applicable.
- **Correct SPL file validation error**
 - If an SPL file cannot be processed because of a validation error, a report on the validation error is sent from FDA to the contact person. Open the SPL file and correct the errors.

Content of Labeling/Listing Scenarios cont...

- **Correct a mistake in an SPL file just submitted**
 - Open the SPL file, correct the mistake, and fill in a **new id root** and **new version number** with the **original setld root** and the appropriate effective time.
- **Update information for a listed drug product**
 - Open the previous SPL file and fill in the new information without changing the other existing information. Fill in a **new id root** and **new version number** with the **original setld root** and the appropriate effective time.

Content of Labeling/Listing

Scenarios cont...

- **Add a new drug product**
 - Open the previous SPL file and fill in the information on a new drug product without changing the information on the other drug products. Fill in a **new** id root and **new** version number with the **original** setId root and the appropriate effective time.
- **Discontinue a previously listed drug product**
 - Open the previous SPL file and update the marketing activity with the expiration date for the last lot released for the specific drug product information without changing the existing information on the other drug products. Fill in a new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time. Once the drug is discontinued, open the most recent SPL file and remove the specific drug product information without changing the existing information on the other drug products. Fill in a new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.

Content of Labeling/Listing Scenarios cont...

- **Change in content of labeling not requiring prior approval**
 - Open the previous SPL file and change the content of labeling without changing the other existing drug listing information. Fill in the new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.
- **Add a package configuration**
 - Open the previous SPL file and add the new package configuration without changing the other existing drug listing information. Fill in the new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.
- **Remove a package configuration**
 - Open the previous SPL file and remove the specific package configuration without changing the other drug listing information. Fill in the new SPL file using a **new** id and **new** version number with the **original** setId and the appropriate effective time.

Submitting SPL R4 Files

- **Naming the file:** The root id from the document identifiers is used for the name of the **SPL** file with the extension “xml”.
- **Sending the file:**
 - SPL files including all associated image files are placed in a **folder** and sent through the FDA Gateway. **One SPL document** (and image files, if applicable) **per folder**.
 - Instructions for using the FDA Gateway are found on the FDA Web site at <http://www.fda.gov/esg>. The name of the “center” and the “type of submission” are used to properly route the files. For electronic drug registration and listing, the center is “OC” and the type of submission is “SPL”.

Pilot Submissions

- FDA has received dozens of official electronic NDC Labeler Code and Establishment Registration submissions since July 2008.
- Quality ranges from good to excellent

Pilot Submissions

Common Errors

- Naming of file (use document root ID)
- Hyphens in the DUNS number (do not use hypens)
- Incorrect Country code (Use ISO-3166)
- Incorrect telephone number format

***Very minor errors

Recommendations

- Review your entire SPL document prior to submission
- Use the current SPL schema, SPL stylesheet, SPL implementation guide, and other SPL technical documents available on the FDA DSC website
- When submitting technical questions regarding SPL XML coding please send an example, if possible.

Participation in Voluntary Pilot Program

- Start with NDC Labeler Code Request
 - Receive feedback from Agency
 - Slowly acclimate to the new electronic eList system
 - Prepare for June 1, 2009

Collaboration with Industry

- HL7 SPL Implementation Working Group
- Drug companies (workshops, individual assistance)
- Vendors (workshops, individual assistance)
- Contact FDA to request 1:1 SPL R4 training sessions

Accomplishments

- FDA (CDER) has been using the SPL standard for almost 3 years
- Quality of SPL documents has improved significantly since October 2005
- DailyMed - **1.6 million** hits per month – (New website less than 3 years old)
- Over **4,039** SPL documents posted on DailyMed (as of October 2008)

Stay Informed

- FDA Data Standards Council website listserv
 - Over **22,000** listserv subscribers as of October 2008
 - <http://www.fda.gov/oc/datacouncil/>



SPL-related Technical Assistance/Questions

- SPL e-mail account (spl@fda.hhs.gov)

Thank you!

Questions?